Methods for detection and elimination of residual human embryonic stem cells in a differentiated cell product

Grant Award Details

Methods for detection and elimination of residual human embryonic stem cells in a differentiated cell product

Grant Type: Early Translational I

Grant Number: TR1-01215

Project Objective: This project addresses the bottleneck of detecting and mitigating the risk of tumorgenicity from a pluripotent cell-derived product candidate. The current project objective is to develop methods to reliably detect and measure the tumorgenicity of a differentiated cell product (pancreatic progenitors) derived from human embryonic stem cell (hESC) and test approaches to mitigate risk of tumor forming cells.

Investigator:

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Institution:	ViaCyte, Inc.
Type:	PI

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Name:	Edouard Stanley
Institution:	Monash University
Type:	Partner-PI

Disease Focus: Diabetes

Collaborative Funder: Victoria, Australia

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $5,405,397

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: NCE

View Report

Grant Application Details

Application Title: Methods for detection and elimination of residual human embryonic stem cells in a differentiated cell product

Public Abstract: Human embryonic stem cells (hESC), and other related pluripotent stem cells, have great potential as starting material for the manufacture of curative cell therapies. This is primarily for two reasons. First, by manipulating cues in their cell culture conditions, these cells can be directed to become essentially any desired human cell type (a property known as pluripotency). Second, hESC have the remarkable capacity to expand rapidly with essentially no change in their identity. At a practical level, this means enough cells to manufacture thousands, and even millions, of therapeutic cell doses can be generated in a matter of weeks. Thus, the biomedical potential is tremendous, but several practical matters remain to be resolved. One of the biggest concerns is that manufacturing processes, i.e., methods to direct “undifferentiated” hESC to become “differentiated” target cell types, have not shown 100% efficiency. That is, some portion of the starting hESC might not differentiate in accordance with the cues given, resulting in a cell therapy product with some contaminating undifferentiated hESC. When undifferentiated hESC are transplanted into animals, they proliferate and differentiate in an uncontrolled, semi-random manner, becoming non-target cell types collectively called a teratoma. Teratomas also occur spontaneously in humans, and consist of a variety of cell types in a disorganized tissue amalgam. Both experimental and spontaneous teratomas are generally benign tumors, and typically can be surgically removed when they become physically problematic due to size or location. While hESC-derived cell therapies have been shown to be effective in animal models of disease, in some instances teratomas have been observed. Thus, the full promise of hESC as source material for novel cell therapies cannot be fully realized until the “teratoma problem” is solved. To date there is no standard method in the field for testing the teratoma potential of a given cell population, nor is there a method for eliminating the potential for teratoma. The proposed project will investigate and establish standardized tests to measure teratoma potential. The tests will be highly sensitive, allowing assurance that large human doses are produced with no risk of teratoma. The project will also investigate a relatively simple method to eliminate undifferentiated hESC in the course of manufacturing. As the last step, the new method will be incorporated into the manufacturing process, the sensitive teratoma tests will be used, and safety data required by the FDA will be collected for a promising new hESC-derived cell therapy for insulin-dependent diabetes. Successful completion of this project will represent a major advance in development of stem cell-derived therapies broadly, and will specifically contribute to the development of a cell therapy for diabetes.

Statement of Benefit to California:	In large part through CIRM initiatives, California hopes to further establish itself as the world center for stem cell research and stem cell-derived therapies. One major issue standing in the way of stem cell-derived therapy development is the possibility of a teratoma forming after transplant with a stem cell-derived cell therapy. A teratoma is a disorganized tissue amalgam containing various different cell types, and is generally a benign tumor. Teratomas can form in animals transplanted with stem cells, and therefore if some stem cells persist in the stem-cell derived therapy, there exists a possibility that teratomas will form in a patient's graft. Indeed, putative stem cells have been found in pre-clinical research-grade stem cell-derived cell therapy preparations, and teratomas have been observed in animals treated with those cells. Currently the conditions favorable to teratoma formation are poorly characterized, and methods to reduce the likelihood of teratoma formation have not been developed. The proposed project will establish standardized sensitive methods to measure the teratoma potential of a cell population, will develop a method to reduce or eliminate teratoma potential, and will include both the method to reduce teratoma and the standard measurement of teratoma potential in the development of an actual prospective cell therapy product for the treatment of insulin-dependent diabetes. If successful, this project will remove a significant bottleneck currently holding the development of stem cell-derived cell therapies back, as well as provide essential pre-clinical data for an important stem cell-derived therapy for diabetes, facilitating its clinical testing in diabetics. The State of California will benefit by playing a key role in removing the teratoma bottleneck from the field, as well as in advancing a promising new cell therapy for diabetes, a disease which directly or indirectly affects millions of Californians. Such a therapy could reduce the state's health care costs tremendously.

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